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A HISTOLOGICAL STUDY OF SENSORY NERVES IN THE LUNG AND THE VISCERAL PLEURA

by

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§ 1 INTRODUCTION

Histological studies of sensory nerves in the lung and the visceral pleura were reported by LARSELL(1923), SUNDER-PLASSMANN(1932), DOW(1933) and S. HAYASHI(1937) etc. LARSELL and DOW(1933), using an intravital methylen-blue technic, described arborized or encapsulated sensory nerve endings here and there in the lung, but in comparison to our histological observation, their descriptions are brief and it seems somewhat differ from our results. SUNDER-PLASSMANN (1932), using Bielschowsky's silver method, recognized the existence of a special nerve ending in the tunica muscularis mucosae of the primary bronchus of the human lung. S. HAYASHI (1937) described this nerve ending more in detail and established the existence of the same type of sensory nerve ending (SETO) in the lung as in the alimentary canal. He also reported a special ending in the lung-parenchyma of the rabbit (Page. 7~8)

Using lungs of human beings and of dogs, I studied the sensory nerves in the lung and the visceral pleura. The results are as follows.

Staining-method

1) SETO's modification of Bielschowsky's silver impregnation (SETO's method) ··· ·····See another print.
2) EHRLICH's staining method of myelin sheaths

§ II SENSORY NERVES IN THE LUNG AND THE VISCERAL PLEURA

1) Sensory nerve endings in the bronchial wall

I found a sensory nerve ending as (SETO) shown in Fig. 1. in the tunica muscularis mucosa of the primary bronchus of the human lung. This nerve fibre is much thicker than autonomic nerves and shows a free termination.

Using EHRLICH's staining method in the tunica muscularis mucosae of the bronchus in the human lung as well as in the dog, I could find no myelinated nerve fibres. I assume, therefore, that this nerve ending has already lost the myelin sheath before entering the tunica muscularis mucosae. I considered it to be a sensory nerve ending, because according to Prof. SETO's description, it shows a typical terminal form (simple free ending).

I found a sensory nerve ending (SETO) also in the epithelium of the primary bronchus of the human lung as shown in Fig. 2. A nerve bundle having a thick fibre appears in the lamina propria ramifying into several branches and enters the epithelium of the bronchus. These nerve branches which run their courses without anastomosing with each other terminate freely between epithelial columnar cells.

2) In the lung-parenchyma of the dog, mainly near the hilum, I found a sensory nerve ending (SETO) which terminates in the alveolar wall, as shown in Fig. 3. A slender nerve fibre A, which branched from a nerve trunk as one of 3 branches, has reached the alveolar wall. Many sensory nerves (SETO) in the lung-parenchyma have been found near the hilum, but in the periphery they rapidly diminish in number.

3) I found a special globule as shown in Fig. 4. near a capillary vessel within the tunica muscularis mucosae of a primary bronchus of the human lung. A nerve fibre undoubtedly thicker than an autonomic nerve enters the globule, showing a tangled ending in it. Fig. 5. is an enlarged figure of the special globule.

4) I found a sensory nerve ending (SETO) as shown in Fig. 6 in the incisura interlobaris of the visceral pleura near the hilum of a dog. This nerve ending shows a few varicosities in the periphery, but clearly has free terminations. Such a nerve ending was not found in the periphery of the visceral pleura except near the hilum. It can be assumed that perhaps this sensory nerve ending (SETO) exists only near the hilum.

5) Near the hilum in the lung of the dog I found myelinated nerve fibres which run between the lung-parenchyma and the visceral pleura. See Fig. 7. This is an example of these myelinated nerve fibres. I can not determine whether they are running from the visceral pleura to the parenchyma or vice versa. At any rate, I am sure that there exists nervous connection by myelinated nerve fibres between both tissues.

6) Using EHRLICH's staining method I found that most of the sensory nerve fibres (SETO) which run into the lung and the visceral pleura have myelin sheaths even into the peri phery as shown in Fig. 8. and 9. Fig. 8. shows a myelinated nerve fibre which branches out in the lamina propria of the bronchus of a dog and Fig. 9. shows one in the visceral pleura near the hilum of a dog.

Most of the sensory nerve fibres in the tunica muscularis mucosae of the bronchial wall have already lost their myelin sheath. Therefore, sensory nerve fibres (SETO) probably lose their thin myelin sheaths only near the termination of their course.

Summry of § II

1) I found sensory nerve endings (SETO) in the lung and the visceral pleura. Most of them had simple and free terminations except a special globule which was found in the tunica muscularis mucosae of a human bronchus.

2) These sensory nerves existed only near the hilum of the lung and visceral pleura and very rarely in the periphery. Near the hilum of the lung the myelinated nerve fibres run between the lung parenchyma and the visceral pleura.

3) These nerves generally were myelinated in these organs and lost their myelin sheaths near their terminations.

4) Using our method I could not find the special types of sensory nerve endings described by SUNDER-PLASSMANN (feines Zäckchen or Endnetze) or by S. HAYASHI (Endkolben or feine nervöse Endnetze).

§ III DEGENERATION OF SENSORY NERVES OF THE LUNG AND THE VISCERAL PLEURA(ESPECIALLY CONCERNING DUAL AFFERENT INNERVATION)

Further experiments were carried out to make clear the composition of the afferent nerve fibres in the lung and the visceral pleura. Using dogs, I cut the nerve trunks and investigated the degeneration of these nerve endings as follows.

1. Unilateral cervical vagotomy in the neck distal to the ganglion nodosum.
2. Section of the unilateral dorsal roots distal to their ganglia (TH_1-TH_5).
3. Bilateral cervical vagotomy distal to the ganglion nodosum.

According to experiments by A. OTSU and N. TANAKA (Kyoto University), myelinated nerve fibres in the stomach or the esophagus disappeared 7 to 9 days after section of their nerve trunks. Therefore, I investigated the degeneration of these nerve endings 4-5 days after the cutting of their nerve trunks.

1) Histological observations of the nerves in the bronchial wall and the visceral pleura on the same side after unilateral vagotomy performed in the neck distal to the ganglion nodosum.

Fig. 10. shows a degenerated nerve fibre in the submucous tissue of the bronchial wall 5 days after unilateral vagotomy on the same side. EHRLICH's staining method.

Fig. 11. shows a degenerated nerve fibre in the tunica propria of the bronchial wall 5 days after unilateral vagotomy on the same side. SETO's modification of BIELSCHOWSKY's silver impregnation. In this figure we can trace a degenerated nerve fibre (axis cylinder) within a small nerve bundle.

Fig. 12. shows a degenerated nerve fibre in the visceral pluera 4 days after unilateral vagotomy on the same side. SETO's modification of Bielschowsky's silver impregnation.

By EHRLICH's staining method I found that most of myelinated nerve fibres of the lung and the visceral pleura showed degeneration 5 days after unilateral cervical

vagotomy on the same side. That is, I found that myelinated nerve fibres distributed in the lung and the visceral pleura were almost vagal in nature.

2) Histological formations of the nerves in the lung and the visceral pleura of dogs in which unilateral vagotomy had been performed in the neck distal to the ganglion nodosum on the contra-lateral side.:

In this experiment I found no degenerated fibres.

3) Histological formation of the nerves in the lung and the visceral pleura of the dog, in which the posterior roots of the spinal cords were cut distal to their ganglia on one side.:

Fig. 13. shows a degenerated nerve fibre on the outside of the cartilagenous ring of the primary bronchus 4 days after section of the homolateral dorsal roots distal to their ganglia (TH_1-TH_5). EHRLICH's staining method.

I only found the degeneration of the faint myelinated nerve fibres within a nerve bundle on the outside of the cartilagenous ring, but I could find such nerve degeneration nowhere inside the cartilagenous ring, in the parenchyma of the lung or in the visceral pleura.

In specimens of lung 5 days after section of the homolateral dorsal roots distal to their ganglia (TH_1-TH_5), I never found a typical figure of degeneration in the myelinated nerve fibres by EHRLICH's staining method.

4) Histological formations of the nerves in the lung and the visceral pleura after bilateral vagotomy in the neck distal to the ganglion nodosum.:

Vagotomy was performed first on the right side and 9 days later on the left side in a dog, then specimens were removed 8 days after the vagotomy on the left side. I found a few myelinated nerve fibres which were still normal in the primary bronchus. They ran across an intercartilagenous space and disappeared inside this space. I could never find myelinated nerve fibres from the inside of the cartilagenous ring to the epithelium. Thick myelinated nerve fibres in nerve bundles on the outside of the bronchial wall had already diminished. In the parenchyma of the lung and the visceral pleura I found no more myelinated nerve fibres.

Summary of § III

1) 5 days after homolateral vagotomy in the neck distal to the ganglion nodosum I found nerve degeneration in the submucous tissue of the bronchial wall and in the visceral pleura. (EHRLICH's staining method and SETO's modification of BIELSCHOWSKY's silver method)

I considered these nerves as vagal, afferent in nature, as later described.

5 days after homolateral cervical vagotomy also I found that most of the myelinated nerve fibres had degenerated in the lung and the visceral pleura. (EHRLICH's staining method)

2) 4 days after section of the homolateral dorsal roots distal to their ganglia (TH_1-TH_5) I found degeneration of the faint myelinated nerve fibres by EHRLICH's staining method within a nerve bundle on the outside of the cartilagenous ring of

the bronchial wall in the lung of a dog.
I think this nerve is a sympathetic afferent nerve, as later described. These degenerated nerve fibres were not found 5 days after homolateral rhizotomy by EHRLICH's staining method.

3) In the lung and the visceral pleura the distribution of the afferent fibres of the vagus is more dense than that of the afferent fibres which come from the nerve cells in the dorsal roots ganglia.

4) Most of the sensory nerve endings (SETO) which were found in the lung and the visceral pleura seem to be vagal in nature.

5) After contralateral vagotomy or rhizotomy I could find no degeneration of the myelinated fibres in the lung and the visceral pleura.

IV CONSIDERATION

Since PHILLIP STOEHR Jr. and K. A. REISER(1932) established their thesis concerning the peripheral structure of the autonomic nervous system-"Terminalreticulum", their thesis has been supported by many authors to this day, although their thesis has raised a few question. Prof. Dr. SETO found a few typical nerve endings which were distinguished from autonomic nerves in the alimentary canal of the human being. He described them as follows.

These nerves have much thicker fibres than autonomic nerves and free terminations. Therefore, they could easily be distinguished from the latter.

From his results, SETO concluded that they must be sensory nerve endings. SETO's nerve endings have found throughout the alimentary canal by many scholars in our laboratory.

As mentioned above, I have also found SETO's nerve endings here and there in the lung and the visceral pleura as well as in the alimentary canal. In regard to sensory nerve endings which were seen in the tunica muscularis mucosae and the epithelium of the bronchial wall of the human lung, SUNDER-PLASSMANN (1932) described them as "Chemoreceptorenfelder" and explained that they conduct impulses of autonomic nerves occurring shock or death during lung-operation. However, he described these nerv terminations as "feines Zäckchen" or "Endnetze" etc. and suggested that they became a network at their peripheral endings.

S. HAYASHI (1937) described the sensory nerve endings in the tunica muscularis mucosae more in detail and observed special nerve terminal forms "Endkolben" or "feine nervöse Endnetze" etc.

Generally sensory nerve fibres are accompanied by small autonomic nerve fibres. Therefore, I think that the distinction between these nerves may be naturally difficult at their peripheral endings.

I could find no such special terminal forms in any sensory nerve endings(SETO) except one special globule which was found in the tunica muscularis mucosae of the human bronchus. Most of the sensory nerve endings (SETO) which 1 found in the lung and the visceral pleura had simple, free terminations.

Recently WEDDELL (1953) established the fact that the sensory nerve (pain,

pressure) terminal forms of cutaneous sensation generally show arborized, free terminations. Therefore, we can say that the sensory nerve terminal forms of the viscera which I found in the lung and the visceral pleura also are generally similar with those of the cutaneous sensation by WEDDELL.

Concerning this point, I think that further investigation is needed. Also S. HAYASHI(1937) described a sensory nerve ending in the lung-parenchyma of the rabbit, but he has not sufficiently described where this nerve terminates.

The sensory nerve ending (SETO) which I found in the lung-parenchyma of the dog clearly reached the alveolar wall.

After posterior rhizotomy (TH_1-TH_5), I recognized that the myelin sheaths of these nerve fibres (SETO) fell into degeneration in the primary bronchus on the outside of the cartilagenous ring. These nerve fibres (SETO) must be considered to run via sympathetic nerves, but they do not change neurones near the sympathetic trunk on the way, as the sympathetic efferents do. Therefore, I believe these nerve fibres (SETO) to be sympathetic afferent nerves; i. e. they are sensory in nature.

The degeneration of the myelinated fibres of the vagus were traced as far as the submucosa or the epithelium of the bronchus. This fact shows that these nerves do not change neurones in the plexus of the bronchial wall, as the vagal efferents do. Therefore, I regard these nerve fibres (SETO) in the vagus as afferent, too.

The movement of the lung is quite passively carried out by the thorax and the diaphragma. According to my histological studies mentioned above, this movement is clearly controlled by impulses through vagal, afferent nerves which exist densely near the hilum of the lung or the visceral pleura and these carry the HERING-BREUER Reflex.

M. TAKINO (1950) described the manner in which muscle spasm of the bronchial wall or hypercapnia of the lung cause a sensation of dyspnea, and he assumed that this sensation was carried by the vagal afferent nerves.

The occurrence of this sensation may be well understood by the existence of vagal sensory endings in the bronchial walls and the alveolar walls as mentioned above.

It has been generally admitted that the lung and the visceral pleura are painless. But I found sensory nerve fibres near the hilum of the lung which come from nerve cells in the dorsal roots ganglia (TH_1-TH_5). Perhaps these nerves terminate near the submucous tissue after losing their myelin sheaths.

It is well known that one can feel slight pain when a large bronchus is stimulated violently or pathologically and this sensation may be due to impulses carried by sensory nerves mentioned above.

N. TANAKA of our clinic has established histologically the dual afferent innervation of the esophagus. The lung and the visceral pleura too are under dual afferent innervation; one is afferent nerve fibres which have their cell bodies in the

dorsal roots ganglia (TH_1-TH_5) (Sympathetic) and the other is the afferent nerve fibres in the vagus.

This fact corresponds well with the results of previous physiological experiments of the lung.

§ V CONCLUSION

Using the lung of human beings and dogs, I studied sensory nerves in the lung and the visceral pleura, and I found the following results.

1) I found sensory nerve endings in the lung and the visceral pleura, not only in the tunica mucosae and the epithelium of the human lung, but also in the lung-parenchyma (in the alveolar wall) and in the visceral pleura of the dog. Most of them had simple and free terminations except a special globule which was found in the tunica muscularis mucosae of the human bronchus.

2) These sensory nerves were found only near the hilum of the lung and the visceral pleura and were very rarely in the peripheral regions. Near the hilum of the lung the myelinated nerve fibres (sensory) run between the lung-perenchyma and visceral pleura.

3) Generally these sensory nerves were myelinated and lost their myelin sheaths near their terminations.

4) Most of these sensory nerve endings (SETO) are vagal, afferent in nature.

5) The lung is under dual afferent innervation.

6) In the lung and the visceral pleura the distribution of the afferent fibres of the vagus is more dense than that of the afferent fibres which have their cell bodies in the dorsal roots ganglia.

7) I did not find myelinated nerve fibres (sensory) which enter the lung and the visceral pleura of the contra-lateral side, running from one side to the other.

(I am much indebted to Assistant Prof. Dr. CHUJI KIMURA of our clinic for his constant help throughout my study.)

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SETO'S MODIFICATION OF BIELSCHOWSKY'S SILVER IMPREGNATION

By
Hachiro Seto

(From the Tohoku Journal of Experimental Medicin. Vol. 54, No. 1, 1951.)

Abstract

1) Fixation more than half an year in 10 per cent neutral formol by adding calcium carbonicum precipitatum in proportion of 1/12. Fixation about 2 to 3 months, when one sectioned the material with the freezing microtome after fixation for 1 to 2 weeks and continued further to fix.

2) A short time in destilled water.

3) 1 to 3 days in 20 per cent silver nitrate fluid.

4) 10 to 20 seconds in destilled water. One should preparate the 5) before passing to the 4) from the 3).

5) One must be ready to make 200 to 300 cc. of 20 per cent neutral formol, which should be made only by diluting the mother neutral formol with running water. This formol solution is divided into 4 to 3 plates. The sections are transferred by turns from the first plate to the last until the white precipitation disappears.

6) Just after washing with running water at a short time, the sections are blotted the water with filter paper and transferred to warming ammonical silver solution, they are stained in it about 10 minutes.

7) Washing 1 to 2 times with destilled water.

8) 3 to 4 hours to a 1/1000 or 1/5000 solution of gold chloride.

9) 15 to 20 per sent natrium hyposulfite, after washing in destilled water.

10) Dehydration and mount in Canada Balsam at last.

EXPLANATION OF THE PLATES

Fig. 1. A sensory nerve ending (Seto) in the t. musc. mucos. of the primary bronchus (Human being). Seto's method. ×640

Fig. 1'. Sketch of Fig. 1. ×640 e...epithelium mm...t. musc. mucos. S...nerve trunk

Fig. 2. A sensory nerve ending (Seto) in the epithelium of the primary bronchus (Human being). Seto's method. ×640

Fig. 2'. Sketch of Fig. 2. ×640 e...epithelium mm...t. musc, mucos. S...nerve trunk

Fig. 3. A sensory nerve ending (Seto) in the lung-parenchyma (Dog). Seto's method. ×640

Fig. 3'. Sketch of Fig. 3. ×640 A...a branch a...alveole

Fig. 4. A special globule within the t. musc. mucos. of the primary bronchus (Human being). Seto's method. ×640

Fig. 4'. Sketch of Fig. 4. ×640 E...epithelium mm...t. musc. mucos. k...small blood vessel

Fig. 5. Enlarged figure of a special globule. 680×10

Fig. 6. A sensory nerve ending (Seto) in the visceral pleura near the hilum (Dog). Seto's method. ×330

Fig. 6'. Sketch of Fig. 6. 330×1/2 p...visceral pleura

Fig. 7. A thick nerve fibre which runs between the lung-parenchyma and the visceral pleura. Seto's method. ×400 p...visceral pleura

Fig. 8. A myelinated nerve fibre which branches out in the t. prop. of the bronchus (Dog). Ehrlich's method. ×400 E...epithelium L.P....t. prop. mm...t. musc. mucos. c...cartil. ring

Fig. 9. A myelinated nerve fibre in the visceral pleura near the hilum (Dog). Ehrlich's method. ×400 p...visceral pleura

Fig. 10. A degenerated nerve fibre in the submucous tissue of the bronchial wall 5 days after homolateral vagotomy (Dog). Ehrlich's method. 80×3

Fig. 11. A degenerated nerve fibre in the t. prop. of the bronchial wall 5 days after homolateral vagotomy (Dog). Seto's method. ×400

Fig. 12. A degenerated nerve fibre in the visceral pleura 4 days after homolateral vagotomy (Dog). Seto's method. 400×3

Fig. 13. A faint degenerated nerve fibre on the outside of the cartilag. ring of the primary bronchus 4 days after section of homolateral dorsal roots distal to their ganglia (TH_1-TH_6) (Dog). Ehrlich's method. 280×3

Fig. 1.

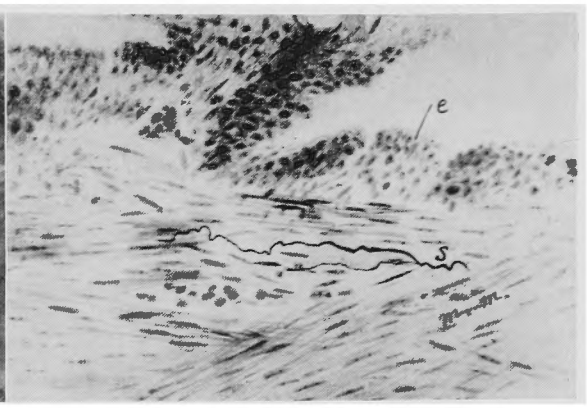


Fig. 1′.

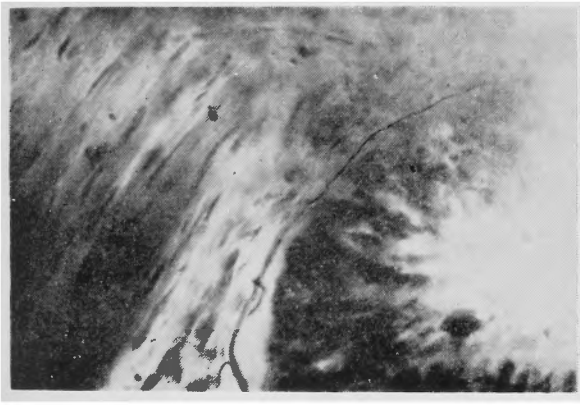
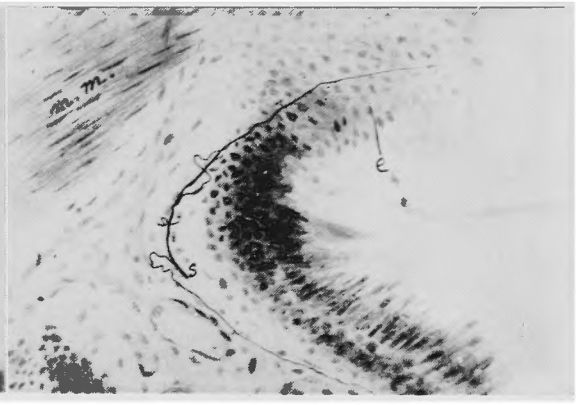


Fig. 2.



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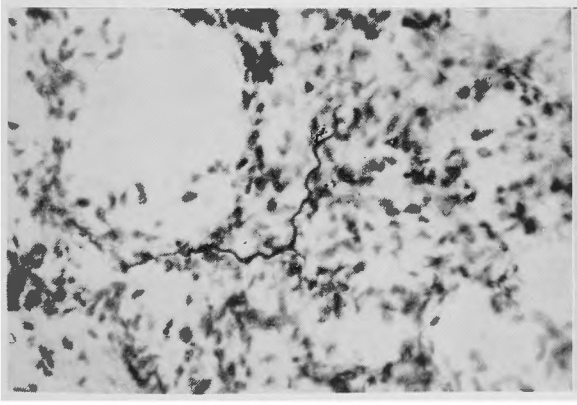

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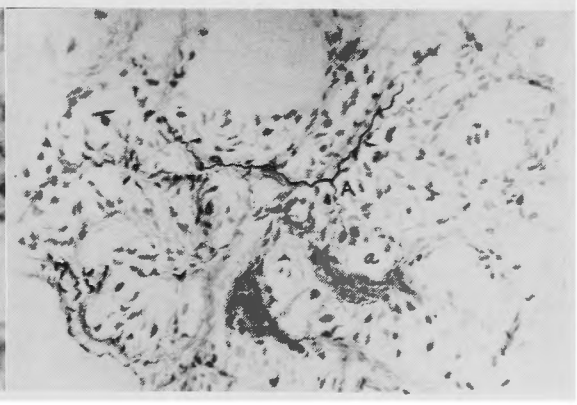

Fig. 3′.

Fig. 4.

Fig. 4'.

Fig. 5.

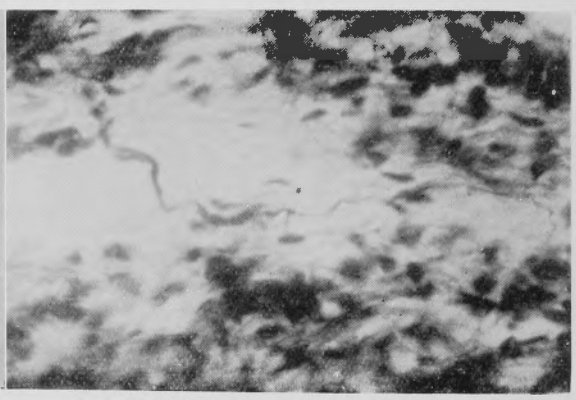

Fig. 6.

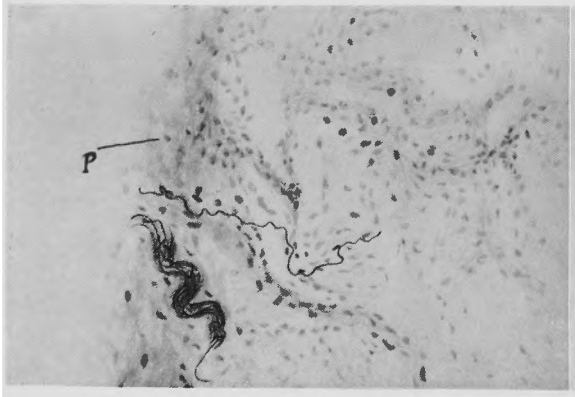

Fig. 7.

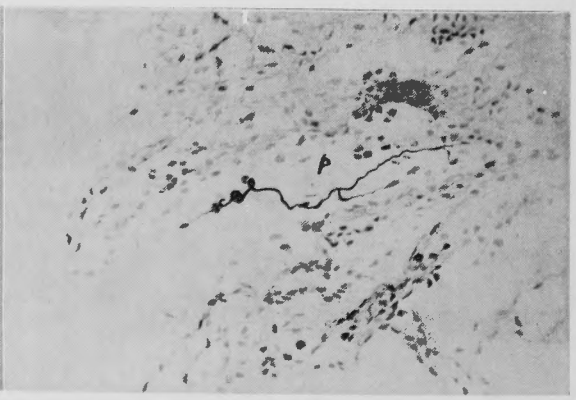

Fig. 6'.

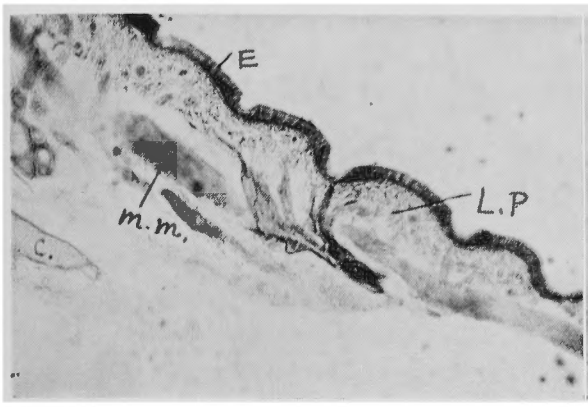

Fig. 8.

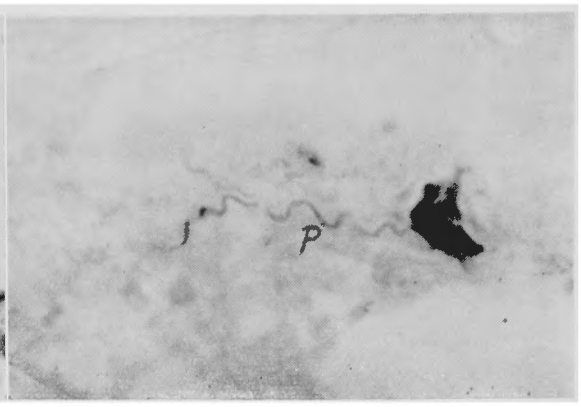

Fig. 9.

Fig. 10.

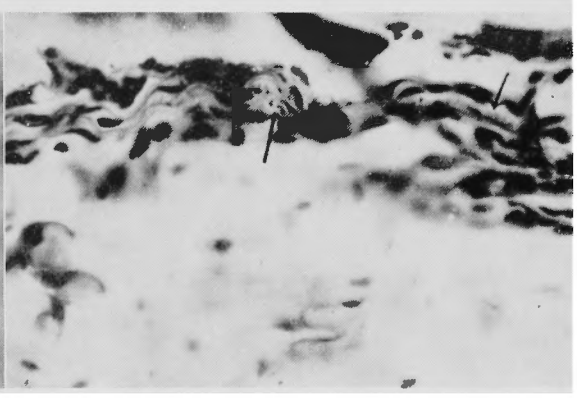

Fig. 11.

Fig. 12.

Fig. 13.

M. YAGITA. III.

和文抄録

肺及び肺肋膜に分布する知覚神経の組織学的研究

京都大学医学部外科学教室第2講座（主任 青柳安誠教授）
八木田 正夫

Bielschowsky—瀬戸氏神経染色法，Ehrlich 氏髄鞘染色法及び迷走神経，背髄後根（Th_1～Th_6）の切断による末梢神経の変性実験より，肺及び肺肋膜内の知覚神経の分布並びにその組成に就き次の結果を得た．

(1) 肺及び肺肋膜に於いては気管支壁粘膜筋層，粘膜上皮内のみならず肺実質内（肺胞壁）（犬），肺肋膜（犬）内に知覚神経終末（瀬戸）を見出した．

此等知覚神経終末の大部分は人肺気管支壁粘膜筋層内に見られた特殊小体を除き単純で遊離性の形態を示している．

(2) 此等知覚神経は肺門附近のみに見出され，周辺部には極めて稀である．

肺門部附近では肺実質と肺肋膜間を走る有髄神経線維（知覚性）が見られる．

(3) 一般に此等知覚神経は有髄性であつて末梢ではその髄鞘を失つている．

(4) 此等知覚神経終末（瀬戸）の大部分は迷走神経中の求心性線維である．

(5) 肺は二重求心性神経支配を受けている．

(6) 肺及び肺肋膜では迷走神経の求心性線維の分布濃度は背髄後根神経節内に神経細胞を有する神経の求心性線維の分布濃度より大である．

(7) 肺及び肺肋膜では一側より他側に交錯して反対側の肺及び肺肋膜に入る有髄神経線維（知覚性）は発見出来なかつた．

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